CLAIMS

What is claimed is:

1. A conformationally restricted polyamine analog of the formula:

E-NH-B-A-B-NH-B-A-B-NH-B-A-B-NH-B-A-B-NH-E

wherein each A is independently selected from the group consisting of: a single bond, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloaryl, and C_3-C_6 cycloalkenyl;

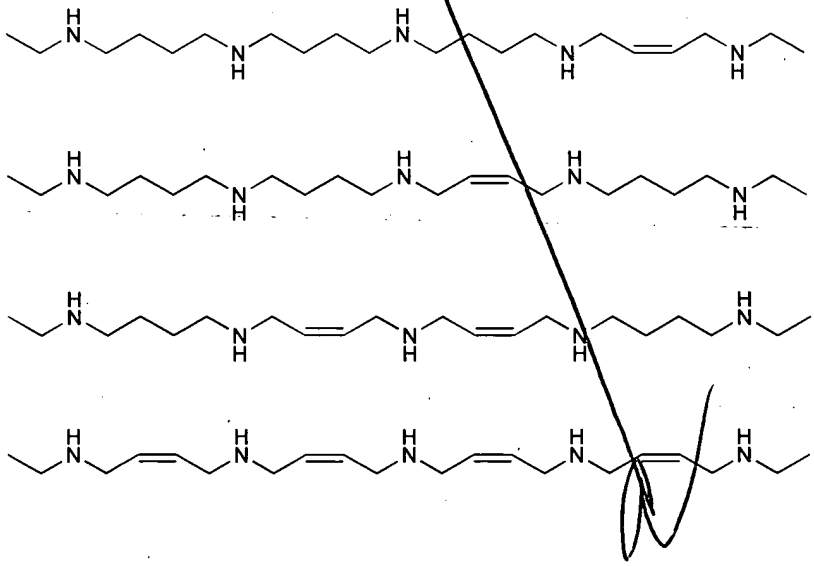
each B is independently selected from the group consisting of: a single bond, C_1-C_6 alkyl, and C_2-C_6 alkenyl;

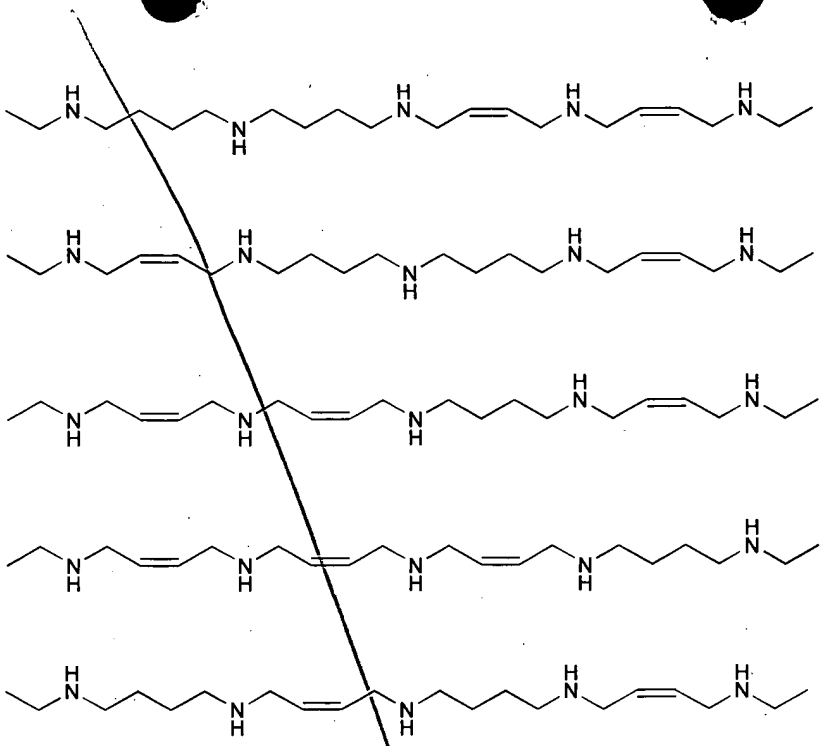
and each E is independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloaryl, and C_3-C_6 cycloalkenyl;

with the proviso that either at least one A moiety is selected from the group consisting of C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloaryl, and C_3-C_6 cycloalkenyl, or at least one B moiety is selected from the group consisting of C_2-C_6 alkenyl;

and any salt or stereoisomer thereof.

2. A conformationally restricted polyamine analog according to claim 1, selected from the group consisting of





, and

, and any salt or stereoisomer thereof.

3. A conformationally restricted polyamine analog of the formula:

E-NH-B-A-B-NH-B-A-B-NH-B-A-B-NH(-B-A-B-NH)$_x$-E

wherein each A is independently selected from the group consisting of: a single bond, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloaryl, and C_3-C_6 cycloalkenyl;

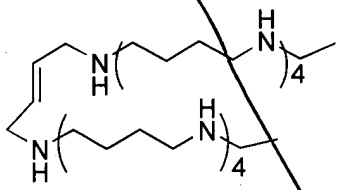
each B is independently selected from the group consisting of: a single bond, C_1-C_6 alkyl, and C_2-C_6 alkenyl;

each E is independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloaryl, and C_3-C_6 cycloalkenyl; and x is an integer from 2 to 16;

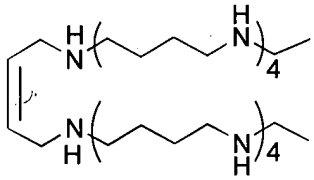
with the proviso that either at least one A moiety is selected from the group consisting of C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloaryl, and C_3-C_6 cycloalkenyl, or at least one B moiety is selected from the group consisting of C_2-C_6 alkenyl;

and any salt or stereoisomer thereof.

4. A conformationally restricted polyamine analog according to claim 3, selected from the group consisting of:



and



;

and any salt or stereoisomer thereof.

5. A polyamine analog of the formula:

E-NH-B-A-B-NH-B-A-B-NH-B-A-B-NH(-B-A-B-NH)$_x$-E

wherein each A is independently selected from the group consisting of: a single bond, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloaryl, and C_3-C_6 cycloalkenyl;

each B is independently selected from the group consisting of: a single bond, C_1-C_6 alkyl, and C_2-C_6 alkenyl;

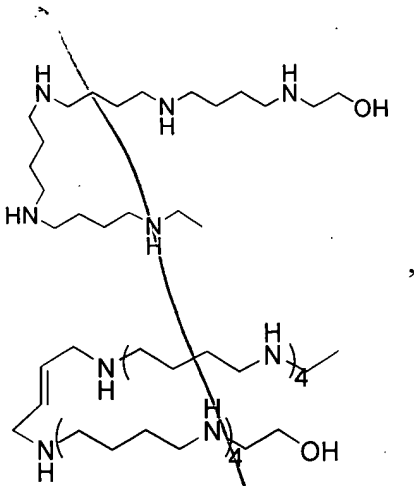
each E is independently selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 alkanol, C_3-C_6 cycloalkanol, and C_3-C_6 hydroxyaryl,

with the proviso that at least one E moiety be selected from the group consisting of C_1-C_6 alkanol, C_3-C_6 cycloalkanol, and C_3-C_6 hydroxyaryl;

and x is an integer from 0 to 16;

and any salt or stereoisomer thereof.

6. A polyamine analog according to claim 5, selected from the group consisting of:



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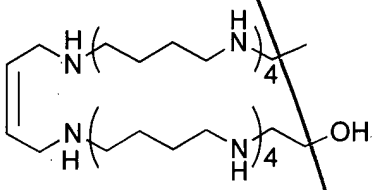


;

and all salts and stereoisomers thereof.

7. A conformationally restricted polyamine analog of the formula:

E-NH-D-NH-B-A-B-NH-D-NH-E

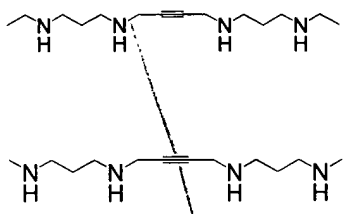
wherein each A is selected from the group consisting of C_2-C_6 alkynyl;

each B is independently selected from the group consisting of: a single bond, C_1-C_6 alkyl, and C_2-C_6 alkenyl;

each D is independently selected from the group consisting of C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkenyl, and C_3-C_6 cycloaryl; and

each E is independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloaryl, and C_3-C_6 cycloalkenyl; and any salt or stereoisomer thereof.

8. A conformationally restricted polyamine analog according to claim 7, selected from the group consisting of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and any salt or stereoisomer thereof.

9. A conformationally restricted polyamine analog of the formula:

E-NH-B-A-B-NH-F-NH-B-A-B-NH-E

wherein F is selected from the group consisting of C_1-C_6 alkyl;

each A is independently selected from the group consisting of: a single bond, C_1-C_6 alkyl; C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloaryl, and C_3-C_6 cycloalkenyl;

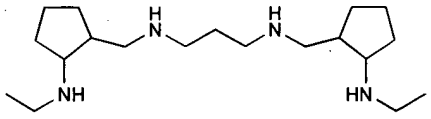
each B is independently selected from the group consisting of: a single bond, C_1-C_6 alkyl, and C_2-C_6 alkenyl; and

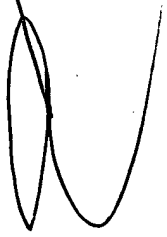
each E is independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloaryl, and C_3-C_6 cycloalkenyl;

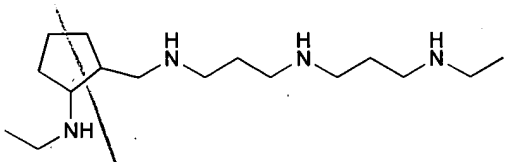
with the proviso that either at least one A moiety is selected from the group consisting of C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloaryl, and C_3-C_6 cycloalkenyl, or at least one B moiety is selected from the group consisting of C_2-C_6 alkenyl;

and any salt or stereoisomer thereof.

10. A conformationally restricted polyamine analog according to claim 9, selected from the group consisting of


and

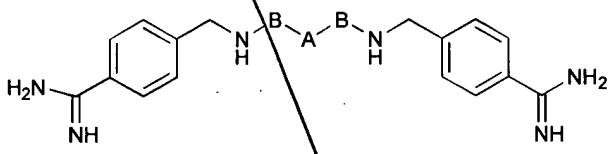




;

and any salt or stereoisomer thereof.

11. A conformationally restricted polyamine analog of the formula:



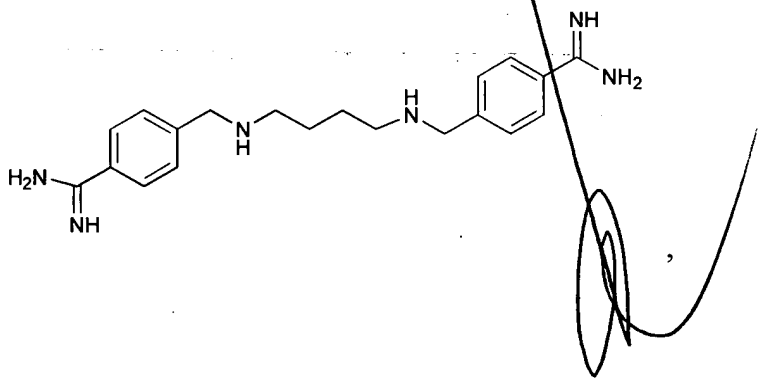
wherein A is independently selected from the group consisting of: a single bond, C_1-C_6 alkyl; C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloaryl, and C_3-C_6 cycloalkenyl;

each B is independently selected from the group consisting of: a single bond, C_1-C_6 alkyl, and C_2-C_6 alkenyl;

with the proviso that A and both B moieties are not all a single bond;

and any salt or stereoisomer thereof.

12. A conformationally restricted polyamine analog according to claim 11, selected from the group consisting of:



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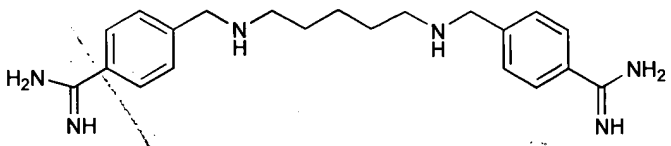
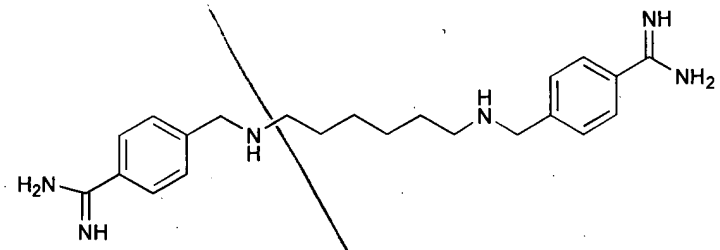


, and



;

and any salt or stereoisomer thereof.

13. A conformationally restricted polyamine analog of the formula:

E-NH-D-NH-B-A-B-NH-D-NH-E

wherein A is selected from the group consisting of C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkenyl, and C_3-C_6 cycloaryl;

each B is independently selected from the group consisting of: a single bond, C_1-C_6 alkyl, and C_2-C_6 alkenyl;

each D is independently selected from the group consisting of C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkenyl, and C_3-C_6 cycloaryl; and

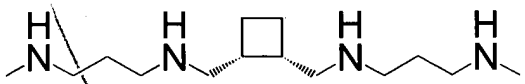
each E is independently selected from the group consisting of H and C_1-C_6 alkyl;

with the proviso that either at least one A moiety is selected from the group consisting of C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloaryl, and C_3-C_6 cycloalkenyl, or at least one B moiety is selected from the group consisting of C_2-C_6 alkenyl;

and the proviso that at least one E is selected from the group consisting of H or methyl;

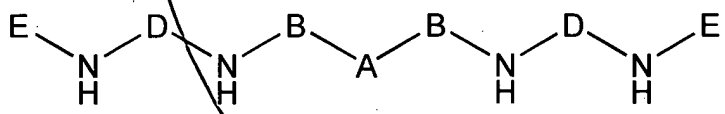
and any salt or stereoisomer thereof.

14. A conformationally restricted polyamine analog according to claim 13 of the formula



and any salt or stereoisomer thereof.

15. A conformationally restricted polyamine analog of the formula:



wherein A is *trans*-ethene

each B is independently selected from the group consisting of: a single bond, C_1-C_6 alkyl, and C_2-C_6 alkenyl;

each D is independently selected from the group consisting of C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloaryl, and C_3-C_6 cycloalkenyl, with the proviso that D is not C_3 alkyl; and

each E is independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloaryl, and C_3-C_6 cycloalkenyl; and any salt thereof.

16. The polyamine analog of claim 1, further comprising a pharmaceutically acceptable excipient.

17. A method of treating an indication in an individual comprising the step of administering to the individual a therapeutic amount of a polyamine analog of claim 1.

18. The method of claim 17, wherein the individual is a human.

19. The method of claim 17, wherein the indication is a cancer.

20. The method of claim 19, wherein the cancer affects cells of the bladder, blood, brain, breast, colon, digestive tract, lung, ovaries, pancreas, prostate gland, or skin.

21. The method of claim 17, wherein the indication is Alzheimer's disease, epilepsy, multiple sclerosis, problems associated with tissue grafts and organ transplants, psoriasis, restenosis, stomach ulcers, or tissue overgrowth after surgery, or an infection or infestation of parasites, bacteria, fungi or insects.

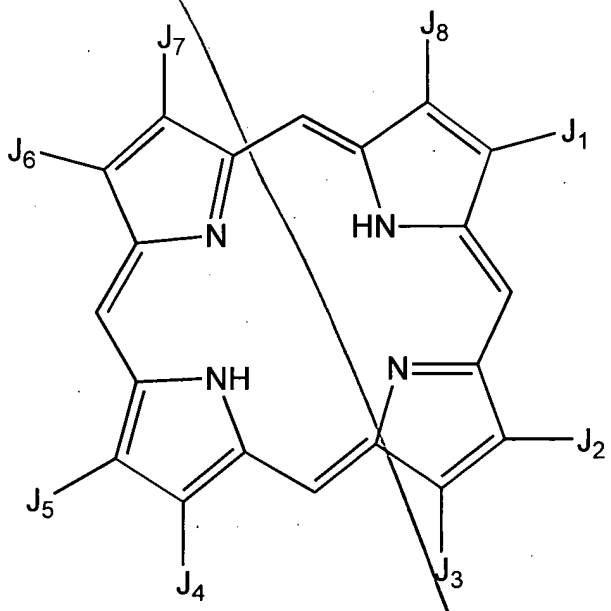
22. A method of suppressing cell growth in an individual comprising the step of administering to the individual a therapeutic amount of a polyamine analog of claim 1.

23. The method of claim 22, wherein the individual is a human.

24. A porphyrin-polyamine conjugate, comprising a polyamine compound covalently linked to a porphyrin compound.

25. A compound of claim 24, wherein the covalent link is an amide bond or a amine bond.

26. A compound according to claim 24 of the formula



wherein at least one of J_1-J_8 is independently selected from the group consisting of

$-K_1-G-L-(N(P)-A)_n-K_2$

where K_1 is independently selected from the group consisting of C_1-C_8 alkyl and where the valence to the left of K_1 attaches to the porphyrin ring;

G is -O-, -(C=O)-, -C(=O)-O-, -O-(C=O)-, -O-(C=O)-O-, -O-(C=O)-N-, -N-(C=O)-O-, or a nonentity;

L is C_1-C_8 alkyl, C_3-C_8 cycloalkyl, C_3-C_8 cycloaryl, C_1-C_8 alkoxy, C_1-C_8 alkyl-C_3-C_8 cycloalkyl, C_1-C_8 alkyl-C_3-C_8 cycloaryl, C_1-C_8 alkoxy-C_3-C_8 cycloaryl, C_3-C_8 cycloalkyl-C_3-C_8 cycloaryl, C_3-C_8 cycloalkyl-C_1-C_8 alkyl, C_3-C_8 cycloaryl-C_1-C_8 alkyl, C_3-C_8 cycloaryl-C_1-C_8 alkoxy, C_3-C_8 cycloaryl-C_3-C_8 cycloalkyl, or a nonentity;

each A is independently selected from the group consisting of C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, C_3-C_8 cycloaryl, C_3-C_8 cycloalkenyl, and C_3-C_8 cycloalkynyl;

P is selected from the group consisting of H and C_1-C_8 alkyl;

n is an integer from 2 to 8;

and K_2 is independently selected from the group consisting of H, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, C_3-C_8 cycloaryl, C_3-C_8 cycloalkenyl, C_3-C_8 cycloalkynyl, C_1-C_8 alkanol, C_3-C_8 cycloalkanol, and C_3-C_8 hydroxyaryl;
where the remainder of the groups J_1-J_8 are each independently selected from the group consisting of H, K_3, or K_4-COOH, where K_3 is independently selected from the group consisting of C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, C_3-C_8 cycloaryl, C_3-C_8 cycloalkenyl, C_3-C_8 cycloalkynyl, C_1-C_8 alkanol, C_3-C_8 cycloalkanol, and C_3-C_8 hydroxyaryl; and K_4 is independently selected from the group consisting of C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, C_3-C_8 cycloaryl, C_3-C_8 cycloalkenyl, and C_3-C_8 cycloalkynyl;
and any salt or stereoisomer thereof.

27. A compound according to claim 26, wherein K_1 and each A are independently selected from the group consisting of C_1-C_8 alkyl, K_2 is independently selected from the group consisting of H and C_1-C_8 alkyl, and the remainder of the groups J_1-J_8 are each independently selected from the group consisting of H, K_3, or K_4-COOH, where K_3 and K_4 are independently selected from the group consisting of C_1-C_8 alkyl.

28. A compound according to claim 27, wherein K_1 is $-CH_2-CH_2-$ or $-CH_2-CH_2-CH_2-$.

29. A compound according to claim 27, wherein n is 4.

30. A compound according to claim 27, wherein J_3, J_4, J_7 and J_8 are independently selected from the group consisting of C_1-C_3 alkyl;
J_5 and J_6 are independently selected from the group consisting of C_1-C_3 alkyl and C_1-C_3 alkyl-COOH;
and J_1 and J_2 are independently selected from the group consisting of C_1-C_3 alkyl-G-N(P_1)-A-(NH-A)$_{n1}$-K_5;
wherein G is -(C=O)- or a nonentity;
P_1 is H or C_1-C_3 alkyl;

each A is independently selected from the group consisting of C_1-C_8 alkyl;

n_1 is 3 or 4;

and K_5 is independently selected from the group consisting of H and C_1-C_8 alkyl.

31. A method of treating an indication in an individual comprising the step of administering to the individual a therapeutic amount of a porphyrin-polyamine conjugate of claim 24.